

REMARKS

Applicants respectfully request reconsideration of the present application in view of the reasons that follow.

I REJECTIONS UNDER 35 U.S.C. § 101

Claims 28, 37, 39, 41, 43, and 45 are rejected under 35 U.S.C. § 101 for a lack of patentable utility. Applicants respectfully traverse the rejection.

The teaching of the application as filed is adequate for a person skilled in the art to readily realize the specific, substantial and credible utility of the present invention as a potential diagnostic marker and a research tool for investigating the pathogenic effects of glycated proteins. Accordingly, applicants disagree with the statement of the last sentence on page 5 of the Office Action that the comparison presented in the application as filed would not be considered substantial evidence regarding diabetes diagnostic utility, unless this comparison is between cells from diabetic and normal control patients. At the time of the present invention, there was no reason for one skilled in the art to expect that *in vitro* results presented in the application would differ from potential *in vivo* results. In fact, Doublier et. al. (Diabetes Vol. 52, April 2003, pp. 1023-1030; attached to this communication) proved that *in vitro* results and *in vivo* results were indeed correlated. In particular, Doublier et. al. demonstrated that glycated albumin reduces the expression level of *nephrin* which supports glomerular functions (abstract and page 1028, right column, lines 6 to 14 from the bottom). Doublier et. al. clearly showed the pathogenic effects of glycated albumin on diabetes, and confirmed the down-regulation of *nephrin* by glycated albumin *in vitro*. In addition, Doublier et. al. showed that the expression level of *nephrin* is reduced in glomeruli of patients (page 1027, left column, last three lines). Based on the above, applicants believe that the specific utility of the invention has been adequately disclosed in the application as filed since there was no reason for one skilled in the art at the time of the invention not to expect the gene, whose expression level is altered by the glycated proteins *in vitro*, to be useful as a potential diagnostic marker and a screening tool for investigating the pathogenic effects of glycated proteins. Furthermore, *in vitro* utility alone constitutes a patentable utility. Accordingly, applicants request withdrawal of the rejection.

Applicants also refer the Examiner to page 407, lines 38-39, of the present application that discloses normal human pulmonary artery endothelial cells used for studying of glycated albumin in cell cultures. Applicants point out that normal cells, in contrast to transformed cell lines, demonstrate the same behavior both *in vitro* and *in vivo*. Thus, although only *in vitro* data are presented in the application, the same behavior is expected *in vivo*. Accordingly, if the Examiner thinks that alteration of HEMBA 1004850 expression level in epithelial cells upon exposure to glycated albumin differs *in vitro* and *in vivo*, specific reasons should be provided.

II REJECTIONS UNDER 35 U.S.C. § 112, first paragraph

Claims 28, 37, 39, 41, 43, and 45 are rejected under 35 U.S.C. § 112, first paragraph, for a lack of enablement. Applicants disagree with the rejection and respectfully traverse it.

Applicants believe that in the rebuttal of the 35 U.S.C. § 101 rejection they proved that the present invention has a specific, substantial, and credible utility as a potential diagnostic marker and a research tool for investigating the pathogenic effects of glycated proteins. In the Office action, the Examiner insists that a substantial utility should be supported by additional evidence regarding the significant expression change differences between diseased and normal genes. Applicants believe that Doublier *et. al.* (Diabetes Vol. 52, April 2003, pp. 1023-1030; attached to this communication) provide this support. Specifically, Doublier *et. al.* show that the expression level of *nephrin* is reduced in glomeruli of patients (page 1027, left column, last three lines). Accordingly, applicants request withdrawal of the rejection.

Applicants believe that the present application is now in condition for allowance. Favorable reconsideration of the application as amended is respectfully requested.

The Examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment,

to Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, as by a check being in the wrong amount, unsigned, post-dated, otherwise improper or informal or even entirely missing, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 19-0741. If any extensions of time are needed for timely acceptance of papers submitted herewith, Applicant hereby petitions for such extension under 37 C.F.R. §1.136 and authorizes payment of any such extensions fees to Deposit Account No. 19-0741.

Respectfully submitted,

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